EXPRESSION PATTERNS OF CELL CYCLE CONTROL GENES IN NON-HODGKIN'S LYMPHOMAS. Howard Wong, Ph.D[1]., Shirley A. Huchcroft, Ph.D[2]., Karl T. Riabowol, Ph.D[1,3] Megan S. Lim, M.D. [1,4], Stefan J. Urbanski, M.D.[4], and Anna E. Kossakowska, M.D.[4], Departments of Medical Biochemistry[1], Epidemiology[2] and Oncology[3], University of Calgary Health Sciences Center, Department of Pathology [4], Foothills Hospital, Calgary, Alberta, Canada.

BACKGROUND: Non-Hodgkin's lymphomas (NHL) represent a heterogeneous group of lymphoid neoplasms that exhibit a diversity of proliferation rates. Proliferative activity, in turn, is normally tightly regulated by a set of cell cycle regulatory genes, which include cyclin-dependent kinases (CDKs) and the genes that regulate their activity, cyclins and cyclin-dependent kinase inhibitors (CDK-inhibitors). Specific patterns of the cell cycle regulatory gene expression that are associated with cellular growth behavior and tumor type/grade may be of prognostic value.

METHODS: We previously developed a sensitive and novel Polymerase Chain Reaction (PCR) method to accurately evaluate mRNA expression. Using this method, we characterized the expression of a set of growth-regulatory genes in thirty-four NHLs. Three D-type cyclins and three CDK inhibitors ($p16^{ink4}$, $p21^{CIP/WAF}$ and p^{27KIP}) were analyzed from each sample, resulting in the generation of tumor-specific RNA-phenotypes that were compared to histological grade and S-phase fraction.

RESULTS: mRNAs encoding a subset of cell cycle genes were found to decrease with increasing tumor grade. At a high level of statistical significance, histological grade was strongly correlated with the levels of cyclin D1 ($P=0.0004$) and $p27^{KIP}$ ($P=0.0005$). In addition, cyclin D2 and $p27^{KIP}$ were inversely correlated with proliferation rates.

CONCLUSIONS: Our results suggest that tumorigenic factors responsible for deregulating cell growth associated with NHL converge upon the cell cycle regulatory apparatus. We propose that an objective molecular assay that monitors gene expression patterns of neoplastic lymphoid cells could aid existing classification schemes, and potentially allow for categorization of currently unclassificable NHLs.

Source: https://www.industrydocuments.ucsf.edu/docs/jgdb0000